

1-methylcyclopropene (1-MCP)  
PC Code 224459  
Type of Review: Human Health and Ecotoxicity

Decision No. 488647  
DP No. 421413  
EPA File Symbol No. : 43813-LT



**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460**

**OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION**

**MEMORANDUM**

**DATE:** January 21, 2015

**SUBJECT:** Science review in Support of the Registration of FYSUIM®, a TGAI/EP  
Containing 98.0 % w/w 1-Methylcyclopropene (1-MCP), As Its Active Ingredient.

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**Chemical Class:** Biochemical  
**PC Code:** 224459  
**CAS Number:** 3100-04-7  
**Tolerance Exemptions:** 40 CFR 180.1220  
**MRID Numbers:** 492650-01 to -06; 492650-40 to -42; 492650-54 & -55; 492650-07  
to -10 & -43; 49265015, 45609001 & 45458608.

**FROM:** Russell S. Jones, Ph.D., Senior Biologist /s/ 01/21/2015  
Biochemical Pesticides Branch  
Biopesticides & Pollution Prevention Division (7511P)

**TO:** Colin Walsh, Regulatory Action Leader /s/ 01/21/2015  
Biochemical Pesticides Branch  
Biopesticides & Pollution Prevention Division (7511P)

**ACTION REQUESTED**

On behalf of Jansen PMP, W. R. Goodwine requests registration of FYSIUM®, containing 98.0 % w/w 1-Methylcyclopropene (1-MCP), an end-use product (which is also the TGAI) intended for

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post-harvest use on apples in enclosed storage facilities. In support of the registration, the applicant submitted product-specific product chemistry information, and is relying on previously reviewed Tier I human health and Tier I environmental fate and effects information submitted by another registrant. Identical product chemistry, human health, and environmental fate and effects information was submitted by Pace International LLC (PACE) in support of an Experimental Use Permit (64864-EUP-E; see Memoranda from R. S. Jones to C. Walsh, dated 05/13/2014 and 07/16/2014).

## RECOMMENDATIONS AND CONCLUSIONS

- 1a. All previously reviewed product chemistry studies submitted or cited in support of Experimental Use Permit 64864-EUP-E (except for the CSF) are deemed ACCEPTABLE to support the registration of FYSIUM® (EPA File Symbol No. 43813-LT; see Memoranda from R. S. Jones to C. Walsh, dated 05/13/2014 and 07/16/2014).
- 1b. The CSF (dated 06/20/2014) for the end-use product must be revised. The sum of the impurities in the TGAI/EP does not equal [REDACTED] and, therefore, the sum of all ingredients on the CSF does not equal 100%. This discrepancy must be resolved.
- 2a. All previously reviewed Tier I Human Health studies submitted or cited in support of Experimental Use Permit 64864-EUP-E are deemed ACCEPTABLE to support the registration of FYSIUM® (EPA File Symbol No. 43813-LT; see Memoranda from R. S. Jones to C. Walsh, dated 05/13/2014 and 07/16/2014). The applicant (Jansen PMP) has provided a copy of an "Offer to Pay" letter to the original data submitter.
- 2b. Toxicological concerns raised by Rohm & Haas Corp., on behalf of Agrofresh, in response to a request for an experimental use permit (64864-EUP-E) by Pace International, LLC, were addressed in the Memorandum from R. S. Jones to C. Walsh, dated 08/19/2014.
- 2c. Range-finding studies conducted by Agrofresh (MRIDs 45380306 & 47024934) also should have been cited by Jansen PMP in support of the registration of FYSIUM®. The aforementioned range-finding studies are necessary preliminary companion studies for the definitive inhalation studies for which an offer to pay was made by Jansen PMP (MRIDs 45609001 & 45458608).
- 3a. A tolerance exemption has been granted for residues of 1-MCP in or on fruits and vegetables (40 CFR 180.1220). The tolerance exemption was supported by residue studies conducted by Rohm & Haas (in support of its Agrofresh subsidiary), that were required by EPA (MRIDs 45380309 & 45609002). See also Memorandum from R. S. Jones to D. Benmhend, dated April, 2001).

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- 3b. EPA required Rohm & Haas to conduct a study that would quantify the amount of 1-MCP that might potentially escape from treated indoor enclosures so as to assess the magnitude of non-worker and non-target organism exposure. The data requirement was fulfilled by a study contained in MRID 45317101.
- 3c. The studies discussed in Conclusions 3a and 3b above were all used by EPA to support the tolerance exemption and should have been cited by Jansen PMP in support of the registration of FYSIUM®.
- 4a. Non-target Organism studies were not submitted. In lieu of nontarget organism studies, the registrant submitted scientific rationales in support of the Series 850 data requirements listed under 40 CFR 158.2060(d). See MRID 49265048. In addition, scientific rationales were submitted for each of the precursor substances (see MRIDs 492650-44, -48, -49, -51, -52, & -53).
- 4b. The rationales are sufficient and ACCEPTABLE to support the data requirements for non-target organisms, provided the current applicant (Jansen PMP) cites the Air Dispersion study contained in MRID 45317101.
- 4c. The Air Dispersion study was the basis for determining that there would be minimal exposure and, therefore, risk to nontarget organisms from inadvertent release of 1-MCP from treated, enclosed facilities. The Air Dispersion study provided the Agency with sufficient information to determine that non-target organisms would not be affected by 1-MCP when the product was used in accordance with EPA-approved product label instructions.
- 4d. The aforementioned studies were requested by the Agency in the Memorandum from R. S. Jones to D. Benmhend, dated 01/29/2002, to support the registration of EPA Reg. No. 71297-1, as well as subsequent AgroFresh/Rohm & Haas products.

## STUDY SUMMARIES

### Tier I Non-Target Organisms (MRIDs 492650-44, -48, -49, -51, -52, & -53)

Tier I non-target organism studies/data/waivers were not submitted. In lieu of studies, the registrant proposed to scientifically credible rationales in support of the Tier I data. The basis for the rationales, as expressed by the applicant, is threefold:

1. 72 FR 60988 (dated 26 October 2007) which references the Non-target Organisms data requirements under 40 CFR 158.2060, specifically test notes 2 and 3, which state:

- Test note 2. "Tests for pesticides intended solely for indoor application would be required on a case-by-case basis, depending on use pattern, physical/chemical properties, production volume, and other pertinent factors;" and
- Test note 3. "Not required for any use groups if the pesticide is highly volatile (estimated volatility  $>5 \times 10^{-5}$  atm m<sup>3</sup>/mol)."

REVIEWER's NOTE: Test Note 3 is only applicable to the data requirements for avian acute toxicity, avian dietary toxicity, fish acute toxicity, and aquatic invertebrate toxicity

2. The 1-MCP BRAD which states:

"Information regarding nontarget organisms was waived based on the minimal exposure to 1-MCP. The enclosed areas treated which originally have a minimal nontarget organisms activity, are fairly gas tight to reduce leakage. As a result, exposure outside the treated areas can also be considered minimal (1-MCP BRAD, p. 5)" and

"The end-use products are intended for use in food and non-food enclosed areas. When applied according to the proposed label, no direct exposure of birds, aquatic organisms and non-target insects to 1-MCP is expected to occur. Thus, 1-MCPs potential environmental/ecological effects are likely to be negligible. As a result, non-target organism/ecological effects studies were not required for this particular use of 1-MCP."

3. Citation of a list of EPA Reg. Nos. for products containing 1-MCP for which non-target organisms studies were waived (EPA Reg. Nos. 71297-1 through 71297-16).

**Other Information Pertaining to the Cited Non-Target Organism Data**

In a Memorandum from R. S. Jones to D. Benmhend, dated 01/29/2002, background information (see Non-Confidential Appendix) was presented, demonstrating that the Agency required the original 1-MCP registrant (AgroFresh/Rohm & Haas) to submit a number of human health and non-target organism/environmental fate studies to support the original tolerance petition for 1-MCP in conjunction with a food use application for EPA Reg. No. 71297-1.

**Conclusions:** The rationales are sufficient and ACCEPTABLE to support the data requirements for non-target organisms, provided the current applicant (Jansen PMP cites the Air Dispersion study contained in MRID 45317101 in support of all indoor uses for EPA Reg. No. 71297-1 (see Conclusions 4a through 4d above). The Air Dispersion study was the basis for determining that there would be minimal exposure and, therefore, risk to nontarget organisms from inadvertent release of 1-MCP from treated, enclosed facilities. The Air

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Dispersion study provided the Agency with sufficient information to determine that non-target organisms would not be affected by 1-MCP when the product was used in accordance with EPA-approved product label instructions.

cc: R.S. Jones, C. Walsh, BPPD Subject File, IHAD  
Russell S. Jones, Ph.D., Sr. Scientist, BPPD/BPB, FT, 01/21/2015

## NON-CONFIDENTIAL APPENDIX

(Copied from Memorandum from R. S. Jones to D. Benmhend, dated 01/29/2002)

### "BACKGROUND

EthylBloc™ (EPA Reg. No. 071297-1) is currently registered for non-food use on floral and nursery crops in enclosed, indoor areas. In support of this registration, the registrant has submitted acceptable product chemistry studies (OPPTS 810.1550-810.7950; Subdivision M Guidelines 151-10 to -17) and acute mammalian toxicity studies [OPPTS 870.1100 to 870.2600; Subdivision M 152-10 to -16 (see Memoranda from R. S. Jones to D. Benmhend, dated 12/23/1998 and 3/1/1999)]; it was also initially concluded that the compound is not a mutagen. No data for non-target organisms and ecological effects were required because the product was not intended for use outdoors or in other non-enclosed areas.

More recently, the registrant requested an experimental use permit (EUP; EPA Reg. No. 71297-EUP-R) to permit the commercial indoor testing of EthylBloc™ on postharvest stored apples (EPA File No. 71297 -1). Under the EUP, the registrant intended to use a maximum of 52.9 lbs of EthylBloc™ (equivalent to 0.074 lbs of 1-MCP) on 10.8 million lbs of post harvested apples. This EUP was deemed acceptable by BPPD (see Memorandum from R. S. Jones to D. Benmhend, dated 9/28/2000) provided it included a crop destruct requirement. The crop destruct requirement was included because there were no established tolerances or tolerance exemptions for residues of 1-MCP on apples or other food commodities.

A petition to establish a permanent exemption from the requirement of tolerances for residues of 1-MCP on food commodities was submitted to the Agency in April 2000 and is the subject of this review. It was noted in the EUP review of 9/28/2000, that since apples are also processed for juice, puree, applesauce, animal feed, etc, that residue data should be used to support the petition for a permanent tolerance exemption for 1-MCP and that these residue data should include data on all raw and processed apple commodities.

On 6/21/2000, a Notice of Filing of a Pesticide Petition to Establish a Tolerance for Certain Pesticide Chemicals in or on All Food Commodities appeared in the Federal Register Volume 65, Number 120; Docket Control No. PF-947), indicating that 1-MCP posed "no significant risk to humans or the environment." In a comment submitted to the Agency (see letter from M. Tichon, Valenti Biosciences Corporation, dated 7/20/2000), it was argued that "the literature indicates risks of adverse effects posed by toxicity of and exposure to 1-MCP are considerably greater than represented in the notice of filing" and that "these risks argue against the issuance of the proposed tolerance exemption. In a letter from S. Longacre to D. Benmhend (dated 12/19/2000), Agrofresh, Inc. submitted a response to these comments including information supporting the registrant's contention that the active ingredient would not cause adverse effects on humans and wildlife when the product is used according to label directions.

The information submitted by AgroFresh, Inc. to support the petition (Petition No. 0F06144) from the requirements of a tolerance for 1-MCP on all food commodities and a label amendment for EthylBloc™ (EPA Reg. No. 071297-1), containing 0.14% 1-MCP as its active ingredient, the comments submitted by Valenti BioSciences (dated 7/20/2000), and AgroFresh's response (dated 12/19/2000) to the Valenti BioSciences comments, were reviewed in a Memorandum from R. S. Jones to D. Benmhend (dated 2/21/2001). In the 2/21/2001 Memorandum, BPPD concurred with the AgroFresh conclusion that when EthylBloc™ (containing 0.14% 1-MCP as its active ingredient) is used according to label directions, exposure to humans and wildlife (by oral, dermal, inhalation, or eye pathways) is extremely low to non-existent. BPPD further concluded that the submitted data/evidence and scientific rationale submitted by AgroFresh indicated that there is a reasonable certainty of no harm with the use of EthylBloc™ (containing 0.14% 1-MCP as its active ingredient) on food commodities stored in closed, sealed treatment facilities and applied according to label directions. However, it is further noted that these determinations were not based upon any quantitative data (generated via guideline or non-guideline studies), but were based upon theoretical calculations.

Therefore, to alleviate concerns regarding 1-MCP residues on treated food, BPPD required the registrant to develop radioisotope techniques to determine whether any 1-MCP (and/or metabolites) remain on treated food after treatment. The registrant was also being required to re-conduct new acute oral toxicity and inhalation studies and the three study battery of genotoxicity/mutagenicity studies. The registrant subsequently submitted an acceptable preliminary analytical method using a Liquid Scintillation Counting (or LSC) method for determining <sup>14</sup>C-1-MCP residues in treated apples; the limit of quantitation was 1 ppb (see Memorandum from R. S. Jones to D. Benmhend, dated 5/03/2001). Accompanying this analytical method, were preliminary residue data obtained from three experiments using apples treated with <sup>14</sup>C-1-MCP. The submitted data, when corrected for mean analytical method recoveries, demonstrated that <sup>14</sup>C-1-MCP residues did not exceed 8.6 ppb in/on apples 24 hours following a 24-hr exposure to 1200 ppb <sup>14</sup>C-1-MCP (1.2x the maximum label application rate). Residues of <sup>14</sup>C-1-MCP were observed to be below the non-radiolabel analytical method detection limit of 10 ppb.

The current submission addresses the new toxicity studies submitted by the registrant to support the tolerance exemption petition and the label amendment to permit the use of the end-use product on food crop. The new toxicity studies were conducted using a new methodology that would assure that the test organisms were exposed to gaseous 1-MCP."